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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/565,100	08/29/2006	Nicola Frances Bateman	056291-5230	6134

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EXAMINER

DICKINSON, PAUL W

ART UNIT	PAPER NUMBER
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1618

MAIL DATE	DELIVERY MODE
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03/18/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/565,100	Applicant(s) BATEMAN ET AL.	
	Examiner PAUL DICKINSON	Art Unit 1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12/05/2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-25 is/are pending in the application.
- 4a) Of the above claim(s) 3, 5, 7 and 17-19 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 4, 6, 8-16 and 20-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's arguments, filed 12/05/2009, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objects are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Double Patenting

The provisional rejection of claims 1-2, 4, 6 and 8-16 on the ground of nonstatutory double patenting over claims 1-18 of copending Application No. 10505231 is maintained for the reasons of record.

Response to Arguments

Claim Rejections - 35 USC § 103

The rejection of claims 1-2, 4, 6 and 8-10, 12-13, 15-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 9633980 (WO '980) in view of US 6096749 ('749) is maintained.

Applicant argues the following:

(1) WO '980 does not teach or suggest a pharmaceutical composition comprising the Agent and a water-soluble acid present as the free acid.

(2) The Injection III example is directed to administration via injection. As amended, claim 1 recites a pharmaceutical composition suitable for oral administration.

(3) '794 discloses thousands of possible formulation options for the compound described therein. There is no indication that hydroxypropylmethylcellulose would be advantageous, or even suitable, for use with compounds such as the Agent.

(4) There is no rationale for modifying the Injection III dosage form of '980 which is directed to administration via injection, to include hydroxypropyl methylcellulose, which is associated in the '794 patent with oral administration dosage forms.

(5) Compound X (encompassing the Agent) is present as 0.1% w/v and the citric acid component is present as 0.38% w/v. Thus, the weight ratio of Agent to acid is 1:3.8 and not 1:35.

(6) There is no motivation or expectation of success in substituting hydroxypropyl methylcellulose for polyethylene glycol.

Applicant's arguments have been fully considered but are not found persuasive for the following reasons:

(1) WO '980 does teach a pharmaceutical composition comprising the Agent and a water-soluble acid present as the free acid, specifically, citric acid (see Injection III).

(2) The recitation of "for oral administration" is an intended use. The recitation of an intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In the instant case, the composition labeled "Injection III" comprises orally acceptable ingredients and is fully capable of being administered orally. Regarding the limitation in claim 16 that the composition be in the

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form of an immediate release tablet, pellet, granules or capsule formulation, the Examiner is interpreting the phrase "Water for injection to 100%" in Injection III to suggest that the other ingredients are mixed first and water is subsequently added. This mixture prior to the addition of water would read on an immediate release granule formulation.

(3) and (6) '749 teaches that hydroxypropyl methylcellulose and polypropylene glycol are functional equivalents as suitable excipients for tyrosine kinase inhibitor formulations. See MPEP § 2144.06.

(4) '794 teaches injection of the tyrosine kinase inhibitor compositions (see col 15, lines 64-67). For parental administration, and specifically for compositions suitable for injection, '794 teaches aqueous solutions of the active agent in combination with water-soluble excipients (see col 16, line 61 to col 17, line 6). It also teaches that stabilizers are often added (see *ibid*). It would be obvious to use the disclosed water-soluble excipients that are suitable for use with tyrosine kinase inhibitors, such as hydroxypropyl methyl cellulose and polyethylene glycol, in the aqueous compositions suitable for injection.

(5) The Examiner agrees that Compound X (encompassing the Agent) is present as 0.1% w/v and the citric acid component is present as 0.38% w/v and the weight ratio is 1:3.8. The Examiner erred in stating that it was 1:35. This value is still within the ratio range recited in the instant claims of 1:1 to 1:10 and the Examiner maintains that it would have been obvious to find the instant range through routine experimentation.

New Grounds of Rejection

Claim Rejections - 35 USC § 112, New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 25 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 25 recites “wherein the composition is a solid at ambient temperature”. Although the instant specification discloses acids which are solid at ambient temperature, it does not support a pharmaceutical composition as recited in claim 1 which is solid at ambient temperature.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

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1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 20-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO9633980 (WO '980; document provided by Applicant) in view of US 6096749 ('749). WO '980 discloses 4-(3'chloro-4'fluoroanilino)-7-methoxy-6-(3-morpholinopropoxy)quinazoline (the Agent), its pharmaceutical formulation, and its role as a tyrosine kinase inhibitor (see abstract; page 4, third paragraph; Example 27). WO '980 teaches one formulation comprising the agent, polyethylene glycol, and citric acid wherein the agent to citric acid ratio is 1:3.8 which satisfies instant claims 21-22 (see Example 32, Injection III). WO '980 teaches that the agent may be in salt or free base form (see Example 32). WO '980 teaches that pharmaceutical formulations of the Agent may be prepared by conventional manners using convention excipients (see

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page 19, fourth paragraph). WO '980 fails to disclose incorporation hydroxypropyl methylcellulose as an excipient.

'749 discloses tyrosine kinase inhibitors and their pharmaceutical formulations (see abstract). '794 teaches injection of the tyrosine kinase inhibitor compositions (see col 15, lines 64-67). For parental administration, and specifically for compositions suitable for injection, '794 teaches aqueous solutions of the active agent in combination with water-soluble excipients (see col 16, line 61 to col 17, line 6). Stabilizers are also often added to the composition (see *ibid*). '749 discloses compounds such as hydroxypropyl methylcellulose and polyethylene glycol as water-soluble excipients suitable for incorporation in tyrosine kinase inhibitor formulations (col 16, lines 1-21).

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to exchange the polyethylene glycol of Injection III for hydroxypropyl methylcellulose, as these two compounds are recognized by the art as functionally equivalent water-soluble excipients suitable for incorporation in tyrosine kinase inhibitor formulations. See MPEP § 2144.05, II.

The recitation of "for oral administration" is an intended use. The recitation of an intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In the instant case, the composition labeled "Injection III" of WO '980 is fully capable of being administered orally.

Claims 1, 11 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO9633980 (WO '980; document provided by Applicant) in view of US 6096749 ('749) in further view of US 5342625 ('625). The relevant portions of WO '980 and '749 are above. WO '980 and '749 fail to teach incorporation of fumaric acid in its free acid form to the formulation.

'625 teaches that citric acid and fumaric acid are known in the art as stabilizers for pharmaceutical compositions administered by injection (see col 16, lines 8-16).

It would have been obvious to one of ordinary skill in the art to substitute the citric acid of Injection III for fumaric acid. The rationale for this is as follows: Citric acid, which is a component in Injection III, is recognized by the art as a stabilizer. That this component is added as a stabilizer is bolstered by '749, which teaches that it is known to add stabilizers to tyrosine kinase inhibitor solutions. Citric acid and fumaric acid are known to serve as stabilizers, and are therefore functional equivalents. It would be obvious to substitute citric acid for fumaric acid in the composition of WO '980, to improve the efficacy of the formulation. See MPEP § 2144.05, II.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to PAUL DICKINSON whose telephone number is (571)270-3499. The examiner can normally be reached on Mon-Thurs 9:00am-6:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

Paul Dickinson
Examiner
AU 1618

March 14, 2009